Calcitropic Non-ionic Surfactant Lamellar Phases

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The aqueous non-ionic surfactant decaethylene glycol hexadecyl ether ($C_{16}EO_{10}$), in the presence of $CaCl_2$, forms novel "calcitropic" lamellar liquid-crystal phases. Thin films of these materials display notable structure sensitivity to the hydrophobicity or hydrophilicity of the underlying support. A structure-bonding model of these materials is based upon Ca^{2+}-crown ether-like coordination to the decaethylene glycol head group of one or two of the surfactant molecules. Ca^{2+} binding of two surfactant head groups, makes possible cis- and trans-conformations for the alkyl tails, resulting in normal and inverted structures with preferences for hydrophilic and hydrophobic surfaces, respectively. The extent of Ca^{2+} ion clustering in the head group determines the geometrical packing requirements of the surfactant and the overall dimensions of the resulting lamellar liquid-crystal phases. The effect of various phosphate reagents (H_3PO_4, KH_2PO_4, K_3PO_4) on these "calcitropic" liquid-crystal phases has also been investigated. The conditions that favor the deposition of different calcium phosphate solid phases from these "calcitropic" lamellar precursors have been investigated, with a view to their possible use as "controlled release biomaterials" for supplying thin-film and nanocrystalline forms of calcium phosphate for bone restoration, replacement, and augmentation applications. The nontoxic, biocompatible, biodegradable, and inexpensive nature of oligoethylene glycol alkyl ethers is a distinctive advantage for these kinds of endeavors.

Introduction

Studies of the structure, dynamics, and applications of surfactant-based micelle and liquid-crystal phases are very well documented.[1] By contrast, the use of these amphiphile assemblies as supramolecular templates for the synthesis of inorganic materials with structures that replicate that of the organic phase is a recent innovation in materials chemistry.[2] In biomineralization, inorganic precursors are deposited at structured organic surfaces to create lithomorphs.[3] Both of these abiological and biological mineralization processes involve the spatially controlled accumulation and reaction of inorganic building blocks at an aqueous−organic interface to form a topological cast of the template. Kresge and co-workers first used this paradigm for the surfactant-based synthesis of mesoporous forms of silica and aluminosilicates.[4] Subsequently the approach was shown to work for other oxide as well as non-oxide-based mesoporous and mesolamellar inorganics, exemplified by tungsten(VI) oxide[5] and tin(IV) sulfide[6] compositions. Templating of inorganic mesostructures has been demonstrated using cationic, anionic, and neutral surfactants.[4,7,8] The mode of formation of these composite mesostructures is the subject of intense study. The current consensus is that the process involves the surfactant-template-facilitated polymerization of inorganic building blocks in a preassembled inorganic−organic mesophase.[8] The inorganic regions are covalently cross-linked in the final replica.

An extension of this synthesis methodology to calcium phosphate-based structures is potentially interesting in terms of biomimicking calcareous mineralization processes in nature as well as producing new types of bone substitutes. However, because ionic bonding interactions dominate in known calcium phosphate phases,[9] different considerations enter into the design and synthesis of mesostructured forms of these materials.

In this paper, chloride-based "calcitropic" non-ionic decaethylene glycol hexadecyl ether ($C_{16}EO_{10}$) liquid-

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crystal phases have been synthesized and characterized for the first time. The deposition of different calcium phosphate solid phases from these liquid-crystal precursors has been investigated, with a view to their possible use as "controlled release biomaterials" for supplying thin-film and nanocrystalline forms of calcium phosphate for bone restoration, replacement, and augmentation applications.[10] This approach takes inspiration from the accepted nontoxic, biocompatible, biodegradable, and inexpensive nature of oligoethylene glycol alkyl ethers,[11] and by comparison with poly(ethylene oxide) salt electrolytes,[12] the anticipated ability of their oligoethylene glycol head groups to sequester Ca^{2+} ions in a pseudo-crown ether-like mode of coordination.[13]

Experimental Section

Materials. Decaethylene glycol hexadecyl ether (Aldrich), calcium chloride dihydrate and potassium phosphate tribasic anhydrous (Fisher), potassium phosphate monobasic anhydrous (BDH), and phosphoric acid (Mallinckrodt, 85%) were used as received. A microscope cover glass, mica, and Teflon were used as substrates for the deposition of mesostructured materials. Their surfaces were prewashed with water and ethanol. A Ca^{2+}-modified glass surface was made by treating a glass microscope slide with an aqueous calcium chloride solution (0.1 M). Silanized glass (i.e., a hydrophobic surface) was made by treating glass microscope slide with a 4% solution of $Si(CH_3)_3Cl$ in $CHCl_3$.

Sample Preparation. The procedure for preparing calcitropic liquid-crystal materials was as follows: an aqueous solution of calcium chloride was added with stirring to an aqueous solution of $C_{16}EO_{10}$ so that the concentration of $C_{16}EO_{10}$ in the final mixture was 40 wt %. The molar ratio $C_{16}EO_{10}/CaCl_2$ was varied. The temperature of mixing was 323 K. The resulting mixture was kept at 298 K for 1 h to 3 days.

The calcitropic liquid-crystal phases were used as growth media for preparing calcium phosphate materials. An aqueous solution of potassium phosphate (or phosphoric acid) was added to the aforementioned mixture of $C_{16}EO_{10}-CaCl_2$ at 323 K. The concentration of $C_{16}EO_{10}$ in the resulting mixture was kept at 40 wt %. This mixture was aged at 298 K for 1−7 days.

The products ($C_{16}EO_{10}-CaCl_2$ and $C_{16}EO_{10}-CaCl_2$-KH_2PO_4 (H_3PO_4 or K_3PO_4) were spread on 323 K preheated substrates and allowed to air-dry at ambient temperature.

Instrumentation. X-ray powder diffraction data of materials, deposited on substrates or packed in a standard sample holder, were obtained on a Siemens D5000 powder diffractometer using Cu Kα radiation and a solid state (Kevex) detector. For routine scans the counting time per step and the step size were 1.5 s and 0.02°, respectively.

Proton-decoupled ^{13}C NMR spectra were acquired at 400 MHz using a Varian VXR 400S spectrometer. Proton-decoupled ^{31}P NMR spectra were recorded at 300 MHz on a Varian GEMINI 300 broad-band spectrometer. The probe temperature on both systems was 298 K. A coaxial insert for 5 mm NMR tubes containing C_6D_6 was used.

Scanning electron microscopy (SEM) and energy-dispersive X-ray fluorescence analysis (EDX) were carried out using a Hitachi S-570 microscope operating at 10−20 kV and equipped with energy-dispersive X-ray fluorescence and elemental microanalysis (Link-1000 computer).

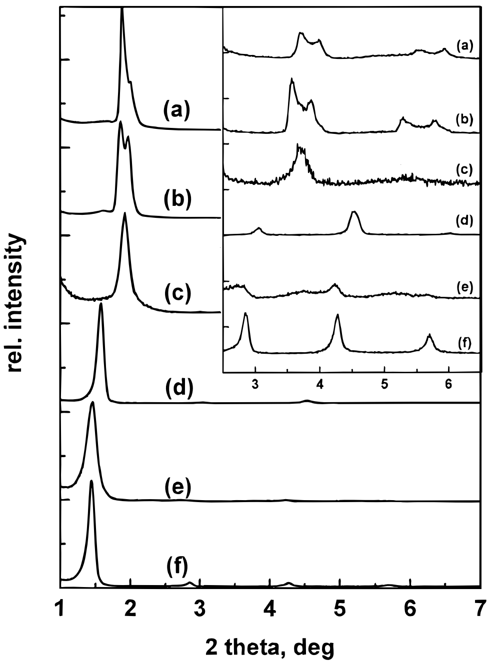

Figure 1. PXRD patterns of $C_{16}EO_{10}-CaCl_2$ air-dried films on glass at different molar ratios of $C_{16}EO_{10}/CaCl_2$: (a) 25/1; (b) 10/1; (c) 2/1; (d) 1/1; (e) 1/1.5; (f) 1/2. Insert: a scale expansion of the low-angle region.

Table 1. Effect of Calcium Chloride Content on the *d* Spacing of Lamellar Liquid-Crystal Phase

molar ratio of ingredients in $C_{16}EO_{10}-CaCl_2$	XRD d_{100} d spacing, Å
25/1	46.7 (43.7[a])
10/1	47.3 (45.0[a])
2/1	46.0
1/1	56.4
1/1.5/	61.0
1/2	61.6
1/3	60.2

[a] Shoulder of lower intensity.

Results and Discussion

Decaethylene Glycol Hexadecyl Ether, $C_{16}EO_{10}$. A glass slide supported film (formed by air-drying an aqueous solution) of the non-ionic surfactant, decaethylene glycol hexadecyl ether, $C_{16}EO_{10}$, displays a PXRD pattern with weak broad (00l) low-angle reflections and distinct narrow high-angle ones. This indicates that the solid surfactant has long-range order of the alkyl chains but short-range order of surfactant bilayers. By contrast, the PXRD pattern of a 40 wt % aqueous film of $C_{16}EO_{10}$ supported on a glass slide, only shows well-defined low-angle (00l) reflections characteristic of an ordered lamellar liquid-crystal phase with short-range ordering of the alkyl chains. The observation of dominant 61.9 Å and minor 53.8 Å d spacings shows that this liquid-crystal phase contains two types of bilayers. Presumably these correspond to either different inclinations of the alkyl ether chains with respect to the lamellae and/or distinct conformations of the decaethylene glycol head group.

Decaethylene Glycol Hexadecyl Ether−Calcium Chloride, $C_{16}EO_{10}-CaCl_2$. At room temperature, 40 wt % aqueous decaethylene glycol hexadecyl ether, $C_{16}EO_{10}$, in the presence of different amounts of $CaCl_2$, forms decaethylene glycol hexadecyl ether−calcium chloride complexes, $C_{16}EO_{10}-CaCl_2$. PXRD studies of

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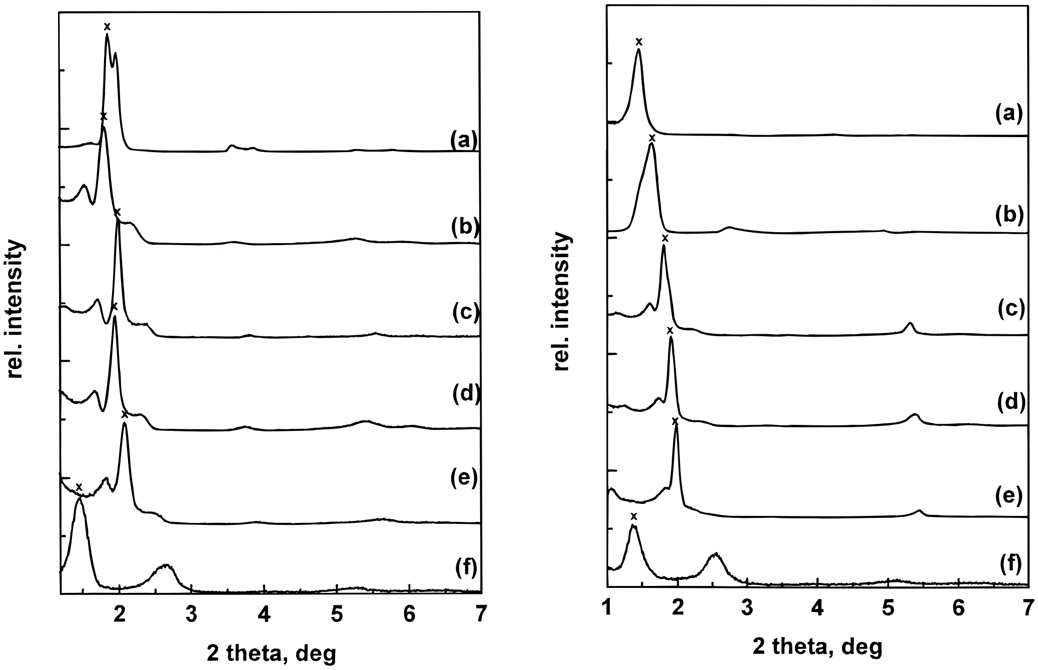

Figure 2. (A, left) PXRD patterns of $C_{16}EO_{10}-CaCl_2$ (molar ratio 10/1) (a−e) air-dried film on different substrates: (a) glass; (b) glass, treated with $CaCl_2$; (c) mica; (d) Teflon; (e) salinized glass; (f) bulk liquid-crystal phase on Plexiglass sample holder. (B, right) PXRD patterns of $C_{16}EO_{10}-CaCl_2$ (molar ratio 1/1.5) (a−e) air-dried film on different substrates: (a) glass; (b) glass, treated with $CaCl_2$; (c) mica; (d) Teflon; (e) salinized glass; (f) bulk liquid-crystal phase on Plexiglass sample holder. The *x* depicts the (001) reflection of the most prominent lamellar phase.

Table 2. Effect of the Type of Substrate on the *d* Spacing of Lamellar Liquid-Crystal Phase

	d spacing $d_{100,}$ Å	
substrate	$C_{16}EO_{10}-CaCl_2$ (10/1)	$C_{16}EO_{10}-CaCl_2$ (1/1.5)
glass	47.3 (45.0[a])	61.0
glass−$CaCl_2$	48.9 (57.4[a])	54.6
mica	44.3 (52.1[a])	48.8 (55.1[a])
Teflon	45.4 (53.4[a])	46.2 (51.6[a])
salinized glass	42.6 (48.8[a])	44.6 (49.3[a])
bulk (0.35mm)	60.4	64.0

[a] Shoulder of lower intensity.

these “calcitropic” liquid-crystal phases in the bulk form (thick film, 0.35 mm), shows the presence of well-ordered lamellae whose *d* spacing depends sensitively on the $CaCl_2$:$C_{16}EO_{10}$ ratio, (Figure 1, Table 1). Below a ratio of 1.5, the interlamellar spacing is ca. 47 Å, at 1.5 it amounts to ca. 56 Å and above this value it is ca. 62 Å. Therefore for $C_{16}EO_{10}-CaCl_2$ ratios in the range 25/1−1/3, at least two distinct calcitropic mesolamellar phases exist.

Noteworthy is the observation that these complexes $C_{16}EO_{10}-CaCl_2$ show considerable structure sensitivity to the hydrophobicity−hydrophilicity of the surface of planar supports, at both high (1.5/1) and low (1/10) loading levels of $CaCl_2/C_{16}EO_{10}$ (Figure 2, Table 2). A hydrophilic substrate (e.g., mica, glass, glass treated with $CaCl_2$) causes a decrease in the interlamellar spacing (for a ca. 50 μm air-dried thin film), of about 9−11 Å relative to the bulk (0.35 mm thick film). For a hydrophobic support (e.g., Teflon, silanized glass), the corresponding decrease is around 15−19 Å.

^{13}C NMR chemical shifts and line widths for different mixtures of $Ca^{2+}/C_{16}EO_{10}$ are given in Figure 3 and Table 3. These observations provide strong evidence for the coordination of Ca^{2+} to the decaethylene glycol head group. The assignments of the linear alkyl chain carbons and the oxyethylene carbons were made on the basis of the data for *n*-dodecyl octaethylene glycol

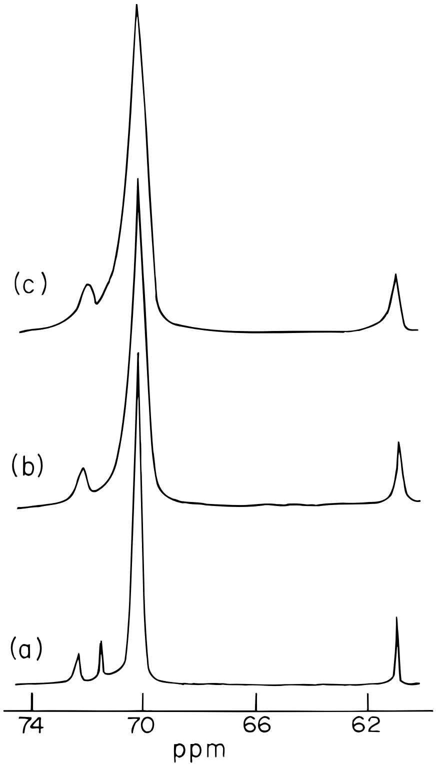

Figure 3. Natural-abundance ^{13}C NMR spectra of the decaethylene glycol chain of the $C_{16}EO_{10}$ liquid-crystal phase (40 wt %) at 400 MHz: (a) without $CaCl_2$; (b) $C_{16}EO_{10}/CaCl_2$ = 1/1; (c) $C_{16}EO_{10}/CaCl_2$ = 1/2, T = 21 °C.

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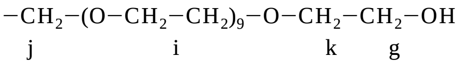
Table 3. ^{13}C NMR Data for the Liquid-Crystal Phase of $C_{16}EO_{10}$ and the Complex $C_{16}EO_{10}-CaCl_2$[a]



$$\underset{j}{-CH_2}-(O-\underset{i}{CH_2-CH_2})_9-O-\underset{k}{CH_2}-\underset{g}{CH_2}-OH$$

	line width, Hz		chemical shift, ppm			
system	j	g	j	k	i	g
$C_{16}EO_{10}$	33.3	8.8	72.3	71.5	70.1	60.9
$C_{16}EO_{10}-CaCl_2$ (10/1)	32.4	12.6	72.5		70.2	61.1
$C_{16}EO_{10}-CaCl_2$ (2/1)	48.8	18.3	72.2		70.1	60.9
$C_{16}EO_{10}-CaCl_2$ (1/1)	51.2	23.2	72.5		70.3	61.2
$C_{16}EO_{10}-CaCl_2$ (1/2)	70.6	23.9		71.7	70.0	60.8

[a] Designation of peak is the same as in ref 14.

monoether[14] in different solvents at 40 °C. The emphasis has been made on the precise differentiation of terminal, penultimate and interior oxyethylene groups, (Table 3). Considerable line broadening is observed for all of the ^{13}C signals of the oligooxyethylene chain, including terminal, interior, and the oxyethylene units next to the alkyl chain, Figure 3. Furthermore, at high content of calcium chloride ($Ca^{2+}/C_{16}EO_{10} = 2/1$), the ^{13}C NMR spectrum loses the peak at 72.2 ppm, assigned as the resonance from the penultimate methylene group. The observed ^{13}C line broadening likely originates from ^{43}Ca ($I = {}^7/_2$) quadrupolar relaxation effects and/or reduction in the rotational correlation times of the ^{13}C nuclei in the oligooxyethylene head group.

Together these results allow one to propose a preliminary structural model for these bulk "calcitropic" liquid-crystal phases. It is based on Ca^{2+}-crown ether-like coordination of the decaethylene glycol head group.[13] Quantification of the slight decrease in pH with Ca^{2+} addition, defines the involvement of 2 equiv of terminal glycol protons at a $CaCl_2$:$C_{16}EO_{10}$ ratio of 1:2. After this point the pH remains essentially constant. This indicates that complexation of the first Ca^{2+} to the decaethylene glycol head group involves the oxygen of the hydroxyl group and some nearest ether oxygens from two surfactants rather than oxygens from one, to produce a charge-neutral $Ca(C_{16}EO_{10})_2Cl_2$ complex. Additional Ca^{2+} coordinates to the remaining head group oxygens yielding $Ca_x(C_{16}EO_{10})_2Cl_{2x}$ complexes. With this model one has the possibility of cis- and trans-isomers for the initially formed $Ca(C_{16}EO_{10})_2Cl_2$ complex, where the cis- and trans- notation designate the relative disposition of the hexadecyl ether tails. Taking the size of a "CaO_n" complex to be ca. 5 Å, then the interlamellar spacing of an untilted $Ca(C_{16}EO_{10})_2Cl_2$ trans lamellar phase is expected to be around 45 Å ($CaCl_2/C_{16}EO_{10} = 1/2$) compared to roughly 50 Å ($CaCl_2/C_{16}EO_{10} = 1/2$) for the cis- analogues. The change in dimension of the head group on coordinating the residual ether oxygens with extra Ca^{2+} in, for example, $Ca_3(C_{16}EO_{10})_2Cl_6$, is difficult to predict. It is envisaged that the change will be small relative to the head-group size in $Ca(C_{16}EO_{10})_2Cl_2$. From these qualitative considerations one anticipates that the extent of Ca^{2+} ion clustering and oxygen coordination in the head group establishes the packing requirements of the surfactant, the relative orientation of the alkyl tails and the overall dimensions of the resulting lamellar liquid-crystal phases.[15]

In the case of the supported liquid-crystal thin films, interfacial surface interactions are able to induce cooperative long-range alterations in the interlayer spacing of the lamellae. Hydrophilic surfaces might preferentially interact with the hydrophilic regions of the "normal" bilayer structure, which are accessible for cis-isomers. On the other hand, hydrophobic surfaces might favor the hydrophobic regions of the "inverted" bilayer structure of the trans- isomer. The significantly smaller interlamellar spacings observed for $Ca_x(C_{16}EO_{10})_2Cl_{2x}$ supported on hydrophobic surfaces such as Teflon indicate that the surfactant bilayers may have indeed been inverted and tilted compared to the situation found for hydrophilic ones such as mica, glass. In the next sections we explore the effect of various phosphate reagents (e.g., H_3PO_4, KH_2PO_4, K_3PO_4) on these "calcitropic" liquid-crystal phases.

Decaethylene Glycol Hexadecyl Ether−Calcium Chloride−Potassium Dihydrogen Phosphate, $C_{16}EO_{10}-CaCl_2-KH_2PO_4$. Without the adjustment of pH in this aqueous ternary system (it changes from 4.1 to 2.5), the PXRD patterns of air-dried thin films on glass slides are characteristic of a lamellar phase, whose interlayer spacing systematically increases with the loading of $CaCl_2$ and KH_2PO_4, from 43.5 to 56.5 Å, (Figure 4A). In this regard the ternary system parallels the behavior of the aqueous binary $C_{16}EO_{10}-CaCl_2$ one, except that there is a contraction of about 3−5 Å in the layer separation. This effect might originate from either the hydrogen-bonding capability of the $H_2PO_4^-$ counteranions to the Ca^{2+}−decaethylene glycol head group, the formation of K^+/Ca^{2+} co-complexes with the decaethylene glycol head group and/or alterations in ion-pair interactions relative to Cl^-. This could lead to a volume contraction of the head group accounting for the observed 3−5 Å decrease in the interlamellar separation.

The appearance of several high-angle PXRD reflections shows the presence of a calcium phosphate solid phase (supported as an air-dried thin film on a glass substrate and a bulk liquid film on a Plexiglass sample holder), which however, could not be identified with a particular structure type, (Figure 4B,C). The SEM EDX of an air-dried sample shows the presence of a matrix of surfactant containing calcium phosphate with a Ca:P ratio of ca. 1:1 (Figure 5A). The ^{31}P NMR spectrum of the binary $C_{16}EO_{10}-KH_2PO_4$ lamellar liquid-crystal phase shows a single resonance at 1.01 ppm with a half-width of 42 Hz, ascribed to the $H_2PO_4^-$ counteranion[16] associated with the K^+-decaethylene glycol head group (Figure 6A, Table 4). The corresponding spectrum for the ternary $C_{16}EO_{10}-CaCl_2$-KH_2PO_4 system is quite distinct showing the ^{31}P NMR resonance shifted upfield to −0.17 ppm (molar ratio $C_{16}EO_{10}/CaCl_2/KH_2PO_4 = 1/1.5/1.5$). The line width gradually increases amounting to 67 Hz in the latter case. The spectrum (d) in Figure 6A consists of two overlapping lines with half-widths of 37 and 94 Hz, respectively. These signals are not resolved in the spectrum (e) of the higher loading sample, although the line width is noticeably broader. The narrower line in spectrum (d) is assigned to the $H_2PO_4^-$ counteranion associated with the Ca^{2+}−decaethylene glycol head group, where the increased shield-

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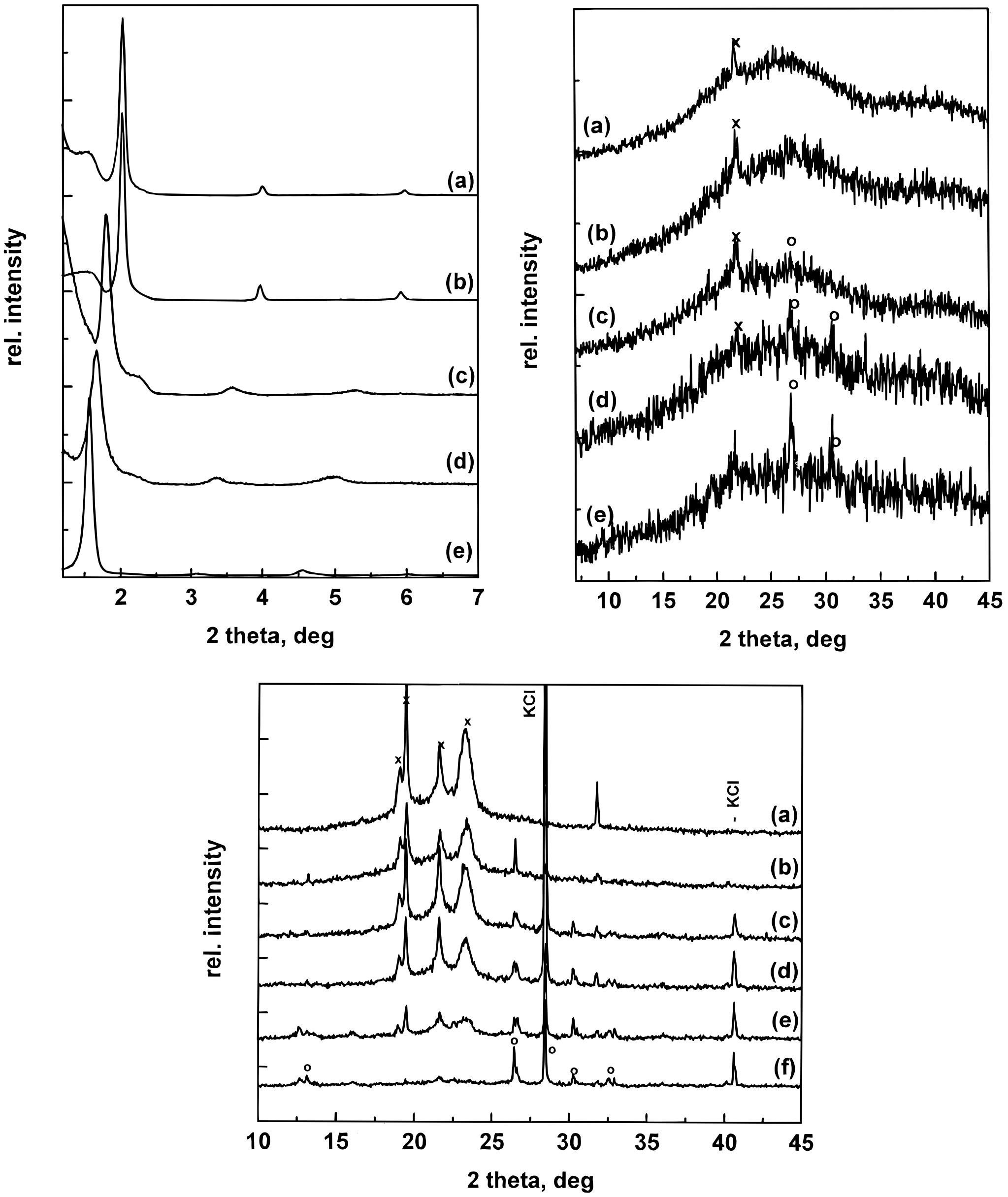

Figure 4. (A) Low-angle PXRD patterns of $C_{16}EO_{10}$–$CaCl_2$-KH_2PO_4 air-dried film on glass at different molar ratio of ingredients: (a) 25/1/1; (b) 10/1/1; (c) 2/1/1; (d) 1/1/1; (e) 1/1.5/1.5. (B) High-angle PXRD patterns of $C_{16}EO_{10}$–$CaCl_2$–KH_2PO_4 air-dried film on glass at different molar ratio of ingredients: (a) 25/1/1; (b) 10/1/1; (c) 2/1/1; (d) 1/1/1; (e) 1/1.5/1.5, (f) 1/2/2. × = surfactant; ○ = calcium phosphate. (C) High-angle PXRD patterns of $C_{16}EO_{10}$–$CaCl_2$–KH_2PO_4 (bulk liquid-crystal phase on Plexiglass sample holder) at different molar ratios of ingredients: (a) 25/1/1; (b) 10/1/1; (c) 2/1/1; (d) 1/1/1; (e) 1/1.5/1.5.

ing compared to K^+ reflects the increased ion-pairing interaction. The broader, more shielded ^{31}P NMR resonance likely originates from the suspended calcium phosphate particles in the liquid-crystal phase.

The observed Ca^{2+} concentration-dependent upfield ^{31}P NMR chemical shifts (Figure 6) is consistent with a model of increased Ca^{2+}–$H_2PO_4^-$ ion-pair clustering in the oligoethylene glycol head group of the calcitropic mesophase. Support for this proposal stems from reports of a similar trend for the effect of Ca^{2+} cation complexation on the ^{31}P chemical shifts of aqueous solutions of phosphates[17] and the assignment of ^{31}P isotropic chemical shifts in solid calcium phosphates.[18]

Decaethylene Glycol Hexadecyl Ether–Calcium Chloride–Orthophosphoric Acid, $C_{16}EO_{10}$–$CaCl_2$–H_3PO_4. This liquid crystal system separates into two layers, a turbid top layer and a transparent bottom layer. There appears to be a competition between calcium ions and protons for binding to the decaethylene glycol head group. Calcium and chloride ions are found in the bottom layer and calcium and phosphate in the top. PXRD shows that the turbid layer is a lamellar liquid-crystal phase whose layer separation is again sensitive to the underlying substrate. The absence of high-angle reflections implies that calcium phosphate does not aggregate into an XRD detectable form (i.e., amorphous, small particle size). The SEM EDX of an air-dried sample on a glass slide shows the presence of a matrix of surfactant containing calcium phosphate with a Ca:P ratio of about 1:1 (Figure 5B).

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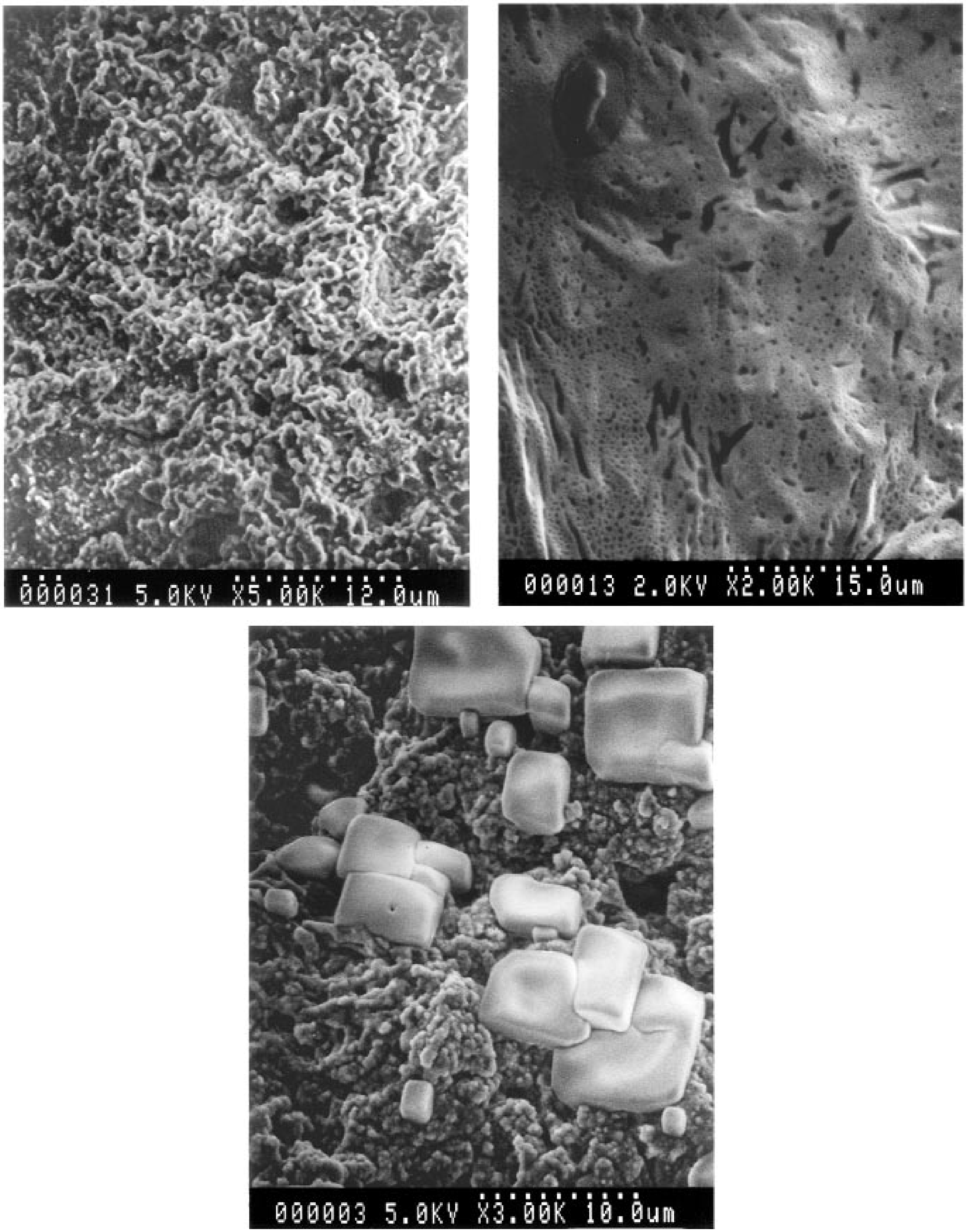

Figure 5. Scanning electron micrographs (SEM) of surfactant containing calcium phosphate (samples on glass slide). (A, top left) Ternary system $C_{16}EO_{10}-CaCl_2-KH_2PO_4$. (B, top right) Ternary system $C_{16}EO_{10}-CaCl_2-H_3PO_4$. (C, bottom) Ternary system $C_{16}EO_{10}-CaCl_2-K_3PO_4$ coexisting with cubic shaped potasium chloride crystals. Dotted scale bar in A = 12 μm, in B = 15 μm, in C = 10 μm.

The bulk $C_{16}EO_{10}-CaCl_2-H_3PO_4$ lamellar phase has a *d* spacing of 58.7 Å, which drops to 55.0−56.5 Å on hydrophilic supports and drops again to 46.7 Å on hydrophobic ones. The parallel behavior to that observed for the $C_{16}EO_{10}-CaCl_2$ lamellar phase suggests that the structure-sensitive surface effect has a common

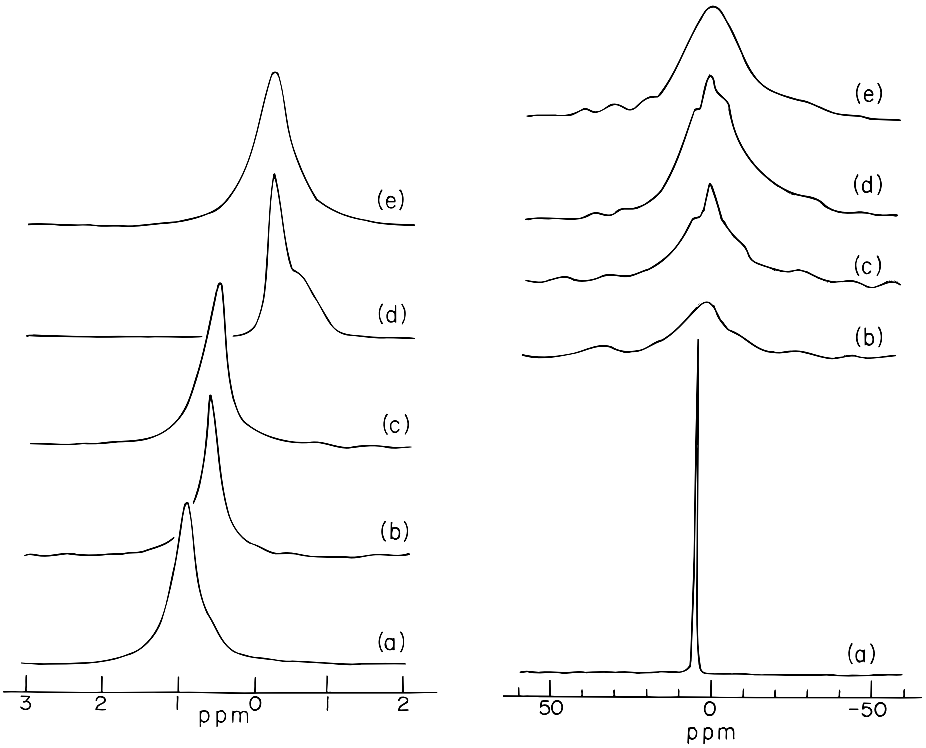

Figure 6. (A) ^{31}P NMR spectra (proton-decoupled, 300 MHz) of $C_{16}EO_{10}-CaCl_2-KH_2PO_4$ as a liquid-crystal phase at different molar ratios of ingredients: (a) 2/0/1; (b) 25/1/1; (c)10/1/1; (d) 1/1/1; (e) 1/1.5/1.5. (B) ^{31}P NMR spectra (proton-decoupled, 300 MHz) of $C_{16}EO_{10}-CaCl_2-K_3PO_4$ as a liquid-crystal phase at different molar ratio of ingredients: (a) 2/0/1; (b) 10/1/1; (c) 2/1/1; (d) 1/1/1; (e) 1/1.5/1.5.

Table 4. ^{31}P NMR Data of Calcium Phosphate in the Liquid-Crystal Phase $C_{16}EO_{10}-CaCl_2-KH_2PO_4$

molar ratio of $C_{16}EO_{10}/CaCl_2/KH_2PO_4$	^{31}P chemical shift, ppm	^{31}P line width, Hz
2/0/1	1.01	41.8
25/1/1	0.66	35.6
10/1/1	0.56	40.4
1/1/1	−0.16	37.1 (94.1[a])
1/1.5/1.5	−0.17	66.8

[a] Shoulder of lower intensity.

origin. A ^{31}P NMR study of $C_{16}EO_{10}-H_3PO_4$ and $C_{16}EO_{10}-CaCl_2-H_3PO_4$ shows a narrow resonance at 0.48 ppm and a structured one at 0.05 ppm, respectively. Further work is needed to identify the nature of the phosphate species in these systems.

Decaethylene Glycol Hexadecyl Ether−Calcium Chloride−Potassium Orthophosphate, $C_{16}EO_{10}-CaCl_2-K_3PO_4$. The ^{31}P NMR spectrum of the binary $C_{16}EO_{10}-K_3PO_4$ liquid-crystal lamellar phase depicts the orthophosphate resonance at 5.04 ppm with a half-width of 58.5 Hz (Figure 6B). A broad resonance centered around 1.3 ppm with a half-width of 2085 Hz and a superimposed sharp signal at 1.25 ppm appears in the ternary $C_{16}EO_{10}-CaCl_2-K_3PO_4$ liquid-crystal phase. The narrow 1.25 ppm line disappears on increasing the calcium chloride and potassium orthophosphate loading. The broad resonance is associated with suspended particles of calcium phosphate which do not sediment from the liquid-crystal phase. This is interesting as these particles appear larger in size than those formed in the $C_{16}EO_{10}-CaCl_2$-KH_2PO_4 system at the same loading. The SEM EDX of an air-dried sample on a glass slide shows the presence of a matrix of surfactant containing calcium phosphate with a Ca:P ratio of ca. 1:1, coexisting with cubic shaped KCl crystals (Figure 5C). It is difficult to ascribe the broad ^{31}P NMR signal to a particular form of calcium phosphate because of the small size and heterogeneity of the particles. These particles show low XRD crystallinity and a pattern that resembles dicalcium phosphate, $CaHPO_4$, with trace amounts of other phases. Interestingly, the narrow ^{31}P NMR signal at 1.25 ppm is in the chemical shift range expected for $H_2PO_4^-$.

Conclusion

The non-ionic surfactant, decaethylene glycol hexadecyl ether, employed in this study plays a multifaceted role: (i) it functions as a multidentate crown ether-like ligand to coordinate and sequester Ca^{2+} into the decaethylene glycol head group region of the surfactant; (ii) it serves as the main building-unit of the resulting "calcitropic" liquid-crystal complexes; (iii) Ca^{2+} binding of two surfactant head groups makes possible cis- and trans-conformations for the alkyl tails, which can result in normal and inverted lamellar phases with different preferences for hydrophylic and hydrophobic surfaces; (iv) it mediates the nucleation and growth of nanocrystalline forms of calcium phosphate upon the addition of phosphate reagents, such as, KH_2PO_4, H_3PO_4, and K_3PO_4.

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